

## AMENDMENTS TO THE CLAIMS

### Listing of Claims

The following listing of claims replaces all previous listings or versions thereof:

1. (original) An isolated specific binding member for human IL-13, comprising an antibody antigen-binding site which is composed of a human antibody VH domain and a human antibody VL domain and which comprises a set of CDR's HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein the VH domain comprises HCDR 1, HCDR2 and HCDR3 and the VL domain comprises LCDR1, LCDR2 and LCDR3, wherein the set of CDR's consists of a set of CDR's selected from the group consisting of:

the BAK278D6 set of CDR's, defined wherein the HCDR1 has the amino acid sequence of SEQ ID NO: 1, the HCDR2 has the amino acid sequence of SEQ ID NO: 2, the HCDR3 has the amino acid sequence of SEQ ID NO: 3, the LCDR1 has the amino acid sequence of SEQ ID NO: 4, the LCDR2 has the amino acid sequence of SEQ ID NO: 5, and the LCDR3 has the amino acid sequence of SEQ ID NO: 6,

a set of CDR's which contains one or two amino acid substitutions compared with the BAK278D6 set of CDR's, and  
each set of CDR's as shown for individual clones in Table 1.

2. (original) An isolated specific binding member according to claim 1 wherein the one or two substitutions are at one or two of the following residues within the CDRs, using the standard numbering of Kabat.

31, 32, 34 in HCDR1

52, 52A, 53, 54, 56, 58, 60, 61, 62, 64, 65 in HCDR2

96, 97, 98, 99, 101 in HCDR3

26, 27, 28, 30, 31 in LCDR1

56 in LCDR2

95A, 97 in LCDR3

3. (original) An isolated specific binding member according to claim 2 wherein the one or two substitutions are made at the following positions from among the identified groups of possible substitute residues for each position:

<u>Position of</u> <u>substitution</u>	<u>Substitute Residue</u> <u>selected from the group</u> <u>consisting of</u>
31 in HCDR1:	Q, D, L, G and E
32 in HCDR1:	T
34 in HCDR1:	V, I and F
52 in HCDR2:	D, N, A, R, G and E
52A in HCDR2:	D, G, T, P, N and Y
53 in HCDR2:	D, L, A, P, T, S, I and R
54 in HCDR2:	S, T, D, G, K and I
56 in HCDR2:	T, E, Q, L, Y, N, V, A, M and G
58 in HCDR2:	I, L, Q, S, M, H, D and K
60 in HCDR2:	R
61 in HCDR2:	R
62 in HCDR2:	K and G
64 in HCDR2:	R
65 in HCDR2:	K
96 in HCDR3:	R and D
97 in HCDR3:	N, D, T and P
98 in HCDR3:	R
99 in HCDR3:	S, A, I, R, P and K
101 in HCDR3:	Y
26 in LCDR1:	D and S

27 in LCDR1: I, L, M, C, V, K, Y, F, R, T, S, A, H and G  
28 in LCDR1: V  
30 in LCDR1: G  
31 in LCDR1: R  
56 in LCDR2: T  
95A in LCDR3: N  
97 in LCDR3: I.

4. (original) An isolated specific binding member according to claim 3 wherein there are two substitutions compared with the BAK278D6 set of CDR's, at HCDR3 residue 99 and LCDR1 residue 27.

5. (original) An isolated specific binding member according to claim 4 comprising the BAK278D6 set of CDR's with a substitution at HCDR3 residue 99 selected from the group consisting of S, A, I, R, P and K, and/or a substitution at LCDR1 residue 27 selected from the group consisting of I, L, M, C, V, K, Y, F, R, T, S, A, H and G.

6. (original) An isolated specific binding member according to claim 4 comprising the BAK278D6 set of CDR's with S substituted for N at HCDR3 residue 99 and/or I substituted for N at LCDR 1 residue 27.

7. (currently amended) An isolated specific binding member according to claim 1 ~~any one of claims 1 to 6~~ wherein HCDR1, HCDR2 and HCDR3 of the VH domain are within a germ-line framework and/or LCDR1, LCDR2 and LCDR3 of the VL domain are within a germ-line framework.

8. (original) An isolated specific binding member according

to claim 7 wherein the HCDR1, HCDR2 and HCDR3 of the VH domain are within germ-line framework VH1 DP14.

9. (currently amended) An isolated specific binding member according to claim 7 ~~or claim 8~~ wherein the HCDR1, HCDR2 and HCDR3 of the VH domain are within germ-line framework VL Vλ3 3h.

10. (currently amended) An isolated specific binding member according to claim 1 ~~any one of claims 1 to 9~~ which binds a human IL-13 variant in which arginine at position 130 is replaced by glutamine.

11. (currently amended) An isolated specific binding member according to claim 1 ~~any one of claims 1 to 10~~ which binds non-human primate IL-13.

12. (original) An isolated specific binding member according to claim 11 wherein the non-human primate IL-13 is rhesus or cynomolgus.

13. (currently amended) A specific binding member according to claim 8 ~~any one of claims 8 to 12~~ comprising the BAK502G9 VH domain (SEQ ID NO: 15).

14. (currently amended) A specific binding member according to claim 8 ~~any one of claims 8 to 13~~ comprising the BAK502G9 VL domain (SEQ ID NO: 16).

15. (currently amended) A specific binding member according to claim 1 ~~any one of claims 1 to 14~~ that binds IL-13 with affinity equal to or better than the affinity of an IL-13

antigen-binding site formed by the BAK502G9 VH domain (SEQ ID NO: 15) and the BAK502G9 VL domain (SEQ ID NO: 16), the affinity of the specific binding member and the affinity of the antigen-binding site being as determined under the same conditions.

16. (currently amended) A specific binding member according to claim 1 ~~any one of claims 1 to 15~~ that neutralizes human IL-13.

17. (original) A specific binding member according to claim 16 that neutralizes human IL-13, with a potency equal to or better than the potency of a IL-13 antigen-binding site formed by the BAK502G9 VH domain (SEQ ID NO: 15) and the BAK502G9 VL domain (SEQ ID NO: 16), the potency of the specific binding member and the potency of the antigen-binding site being as determined under the same conditions.

18. (currently amended) A specific binding member according to claim 1 ~~any one of claims 1 to 17~~ that comprises an scFv antibody molecule.

19. (currently amended) A specific binding member according to claim 1 ~~any one of claims 1 to 17~~ that comprises an antibody constant region.

20. (original) A specific binding member according to claim 19 that comprises a whole antibody.

21. (original) A specific binding member according to claim 20 wherein the whole antibody is IgG4.

22. (currently amended) An isolated antibody VH domain of a specific binding member according to claim ~~any one of claims 1 to 21~~.

23. (currently amended) An isolated antibody VL domain of a specific binding member according to claim ~~any one of claims 1 to 21~~.

24. (currently amended) A composition comprising a specific binding member, antibody VH domain or antibody VL according to claim ~~any one of claims 1 to 23~~, and at least one additional component.

25. (original) A composition according to claim 24 comprising a pharmaceutically acceptable excipient, vehicle or carrier.

26. (currently amended) An isolated nucleic acid which comprises a nucleotide sequence encoding a specific binding member or antibody VH or VL domain of a specific binding member according to claim ~~any one of claims 1 to 23~~.

27. (original) A host cell *in vitro* transformed with nucleic acid according to claim 26.

28. (original) A method of producing a specific binding member or antibody VH or VL domain, the method comprising culturing host cells according to claim 27 under conditions for production of said specific binding member or antibody VH or VL domain.

29. (original) A method according to claim 28 further

comprising isolating and/or purifying said specific binding member or antibody VH or VL variable domain.

30. (currently amended) A method according to claim 28 ~~or claim 29~~ further comprising formulating the specific binding member or antibody VH or VL variable domain into a composition including at least one additional component.

31. (original) A method for producing an antibody antigen-binding domain specific for human IL-13, the method comprising providing, by way of addition, deletion, substitution or insertion of one or more amino acids in the amino acid sequence of a parent VH domain comprising HCDR 1, HCDR2 and HCDR3, wherein the parent VH domain HCDR1, HCDR2 and HCDR3 are the BAK278D6 set of HCDR's, defined wherein the HCDR1 has the amino acid sequence of SEQ ID NO: 1, the HCDR2 has the amino acid sequence of SEQ ID NO: 2, the HCDR3 has the amino acid sequence of SEQ ID NO: 3, or the BAK502G9 set of HCDR's, defined wherein the HCDR1 has the amino acid sequence of SEQ ID NO: 7, the HCDR2 has the amino acid sequence of SEQ ID NO: 8, the HCDR3 has the amino acid sequence of SEQ ID NO: 9, a VH domain which is an amino acid sequence variant of the parent VH domain, and optionally combining the VH domain thus provided with one or more VL domains to provide one or more VH/VL combinations; and

testing said VH domain which is an amino acid sequence variant of the parent VH domain or the VH/VL combination or combinations to identify an antibody antigen binding domain specific for human IL-13.

32. (original) A method according to claim 31 wherein the parent VH domain amino acid sequence is selected from the

group consisting of SEQ ID NO: 13 and SEQ ID NO: 15.

33. (currently amended) A method according to claim 31 ~~or claim 32~~ wherein said one or more VL domains is provided by way of addition, deletion, substitution or insertion of one or more amino acids in the amino acid sequence of a parent VL domain comprising LCDR 1, LCDR2 and LCDR3, wherein the parent VL domain LCDR1, LCDR2 and LCDR3 are the BAK278D6 set of LCDR's, defined wherein the LCDR1 has the amino acid sequence of SEQ ID NO: 4, the LCDR2 has the amino acid sequence of SEQ ID NO: 5, the LCDR3 has the amino acid sequence of SEQ ID NO: 6, or the BAK502G9 set of LCDR's, defined wherein the LCDR1 has the amino acid sequence of SEQ ID NO: 10, the LCDR2 has the amino acid sequence of SEQ ID NO: 11, the LCDR3 has the amino acid sequence of SEQ ID NO: 12, producing one or more VL domains each of which is an amino acid sequence variant of the parent VL domain.

34. (original) A method according to claim 33 wherein the parent VL domain amino acid sequence is selected from the group consisting of SEQ ID NO: 14 and SEQ ID NO: 16.

35. (original) A method for producing an antibody antigen-binding domain specific for human IL-13, the method comprising providing, by way of addition, deletion, substitution or insertion of one or more amino acids in the amino acid sequence of a parent VH domain comprising HCDR 1, HCDR2 and HCDR3, wherein the parent VH domain HCDR1, HCDR2 and HCDR3 are the BAK167A11 set of HCDR's, defined wherein the HCDR1 has the amino acid sequence of SEQ ID NO: 55, the HCDR2 has the amino acid sequence of SEQ ID NO: 56, the HCDR3 has the amino acid sequence of SEQ ID NO: 57, the BAK615E3 set of HCDR's, defined



wherein the HCDR1 has the amino acid sequence of SEQ ID NO: 153, the HCDR2 has the amino acid sequence of SEQ ID NO: 154, the HCDR3 has the amino acid sequence of SEQ ID NO: 155, the BAK582F7 set of HCDR's, defined wherein the HCDR1 has the amino acid sequence of SEQ ID NO: 141, the HCDR2 has the amino acid sequence of SEQ ID NO: 142, the HCDR3 has the amino acid sequence of SEQ ID NO: 143, or the BAK612B5 set of HCDR's, defined wherein the HCDR1 has the amino acid sequence of SEQ ID NO: 147, the HCDR2 has the amino acid sequence of SEQ ID NO: 148, the HCDR3 has the amino acid sequence of SEQ ID NO: 149, a VH domain which is an amino acid sequence variant of the parent VH domain, and optionally combining the VH domain thus provided with one or more VL domains to provide one or more VH/VL combinations; and

testing said VH domain which is an amino acid sequence variant of the parent VH domain or the VH/VL combination or combinations to identify an antibody antigen binding domain specific for human IL-13.

36. (original) A method according to claim 35 wherein the parent VH domain amino acid sequence is selected from the group consisting of SEQ ID NO: 55 and SEQ ID NO: 33.

37. (currently amended) A method according to claim 35 ~~or claim 36~~ wherein said one or more VL domains is provided by way of addition, deletion, substitution or insertion of one or more amino acids in the amino acid sequence of a parent VL domain comprising LCDR 1, LCDR2 and LCDR3, wherein the parent VL domain LCDR1, LCDR2 and LCDR3 are the BAK167A11 set of LCDR's, defined wherein the LCDR1 has the amino acid sequence of SEQ ID NO: 58, the LCDR2 has the amino acid sequence of SEQ ID NO: 59, the LCDR3 has the amino acid sequence of SEQ ID NO:

60, the BAK615E3 set of LCDR's, defined wherein the LCDR1 has the amino acid sequence of SEQ ID NO: 156, the LCDR2 has the amino acid sequence of SEQ ID NO: 157, the LCDR3 has the amino acid sequence of SEQ ID NO: 158, the BAK582F7 set of LCDR's, defined wherein the LCDR1 has the amino acid sequence of SEQ ID NO: 144, the LCDR2 has the amino acid sequence of SEQ ID NO: 145, the LCDR3 has the amino acid sequence of SEQ ID NO: 146, or the BAK612B5 set of LCDR's, defined wherein the LCDR1 has the amino acid sequence of SEQ ID NO: 150, the LCDR2 has the amino acid sequence of SEQ ID NO: 151, the LCDR3 has the amino acid sequence of SEQ ID NO: 152, producing one or more VL domains each of which is an amino acid sequence variant of the parent VL domain.

38. (original) A method according to claim 37 wherein the parent VL domain amino acid sequence is selected from the group consisting of SEQ ID NO: 24 and SEQ ID NO: 34.

39. (currently amended) A method according to claim 31~~any one of claims 31 to 34~~ wherein said VH domain which is an amino acid sequence variant of the parent VH domain is provided by CDR mutagenesis.

40. (currently amended) A method according to claim 35~~any one of claims 35 to 38~~ wherein said VH domain which is an amino acid sequence variant of the parent VH domain is provided by CDR mutagenesis.

41. (currently amended) A method according to claim 31~~any one of claims 31 to 40~~ further comprising providing the antibody antigen binding site within an IgG, scFv or Fab antibody molecule.

42. (original) A method of producing a specific binding member that binds human IL-13, which method comprises:

providing starting nucleic acid encoding a VH domain or a starting repertoire of nucleic acids each encoding a VH domain, wherein the VH domain or VH domains either comprise a HCDR1, HCDR2 and/or HCDR3 to be replaced or lack a HCDR1, HCDR2 and/or HCDR3 encoding region;

combining said starting nucleic acid or starting repertoire with donor nucleic acid or donor nucleic acids encoding or produced by mutation of the amino acid sequence of the HCDR1 (SEQ ID NO: 1) or HCDR1 (SEQ ID NO: 7), HCDR2 (SEQ ID NO: 2) or HCDR2 (SEQ ID NO: 8) and/or HCDR3 (SEQ ID NO: 3) or HCDR3 (SEQ ID NO: 9) such that said donor nucleic acid is or donor nucleic acids are inserted into the CDR1, CDR2 and/or CDR3 region in the starting nucleic acid or starting repertoire, so as to provide a product repertoire of nucleic acids encoding VH domains;

expressing the nucleic acids of said product repertoire to produce product VH domains;

optionally combining said product VH domains with one or more VL domains;

selecting a specific binding member specific for human IL-13, which specific binding member comprises a product VH domain and optionally a VL domain; and

recovering said specific binding member or nucleic acid encoding it.

43. (original) A method according to claim 42 wherein the donor nucleic acids are produced by mutation of said HCDR1 and/or HCDR2.

44. (original) A method according to claim 42 wherein the

donor nucleic acid is produced by mutation of HCDR3.

45. (original) A method according to claim 44 comprising providing the donor nucleic acid by mutation of nucleic acid encoding the amino acid sequence of HCDR3 (SEQ ID NO: 3) or HCDR3 (SEQ ID NO: 9).

46. (original) A method according to claim 42 comprising providing the donor nucleic acid by random mutation of nucleic acid.

47. (currently amended) A method according to claim 42~~any one of claims 42 to 46~~ further comprising attaching a product VH domain that is comprised within the recovered specific binding member to an antibody constant region.

48. (currently amended) A method according to claim 42~~any one of claims 42 to 46~~ comprising providing an IgG, scFv or Fab antibody molecule comprising the product VH domain and a VL domain.

49. (currently amended) A method according to claim 31~~any one of claims 31 to 48~~, further comprising testing the antibody antigen-binding domain or specific binding member that binds human IL-13 for ability to neutralize human IL-13.

50. (original) A method according to claim 49 wherein a specific binding member that comprises an antibody fragment that binds and neutralizes human IL-13 is obtained.

51. (original) A method according to claim 50 wherein the antibody fragment is an scFv antibody molecule.

52. (original) A method according to claim 50 wherein the antibody fragment is an Fab antibody molecule.

53. (currently amended) A method according to claim 51 ~~or claim 52~~ further comprising providing the VH domain and/or the VL domain of the antibody fragment in a whole antibody.

54. (currently amended) A method according to claim 31~~any one of claims 31 to 53~~ further comprising formulating the specific binding member that binds IL-13, antibody antigen-binding site or an antibody VH or VL variable domain of the specific binding member or antibody antigen-binding site that binds IL-13, into a composition including at least one additional component.

55. (currently amended) A method according to claim 31~~any one of claims 31 to 54~~ further comprising binding a specific binding member that binds human IL-13 to IL-13 or a fragment of IL-13.

56. (currently amended) A method comprising binding a specific binding member that binds IL-13 according to claim 1~~any one of claims 1 to 21~~ to human IL-13 or a fragment of human IL-13.

57. (currently amended) A method according to claim 55 ~~or claim 56~~ wherein said binding takes place *in vitro*.

58. (currently amended) A method according to claim 55~~any one of claims 55 to 57~~ comprising determining the amount of binding of specific binding member to IL-13 or a fragment of IL-13.

59. (currently amended) A method according to claim 31~~any one of claims 31 to 58~~ further comprising use of the specific binding member in the manufacture of a medicament for treatment of a disease or disorder selected from the group consisting of asthma, atopic dermatitis, allergic rhinitis, fibrosis, inflammatory bowel disease and Hodgkin's lymphoma.

60. (currently amended) Use of a specific binding member according to claim 20~~any one of claims 1 to 21~~ in the manufacture of a medicament for treatment of a disease or disorder selected from the group consisting of asthma, atopic dermatitis, allergic rhinitis, fibrosis, inflammatory bowel disease and Hodgkin's lymphoma.

61. (currently amended) A method of treatment of a disease or disorder selected from the group consisting of asthma, atopic dermatitis, allergic rhinitis, fibrosis and Hodgkin's lymphoma, the method comprising administering a specific binding member according to claim 1~~any one of claims 1 to 21~~ to a patient with the disease or disorder or at risk of developing the disease or disorder.

62. (original) An isolated specific binding member for human IL-13, comprising an antibody antigen-binding domain site which is composed of a human antibody VH domain and a human antibody VL domain and which comprises a set of CDR's, HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein the VH domain comprises HCDR1, HCDR2 and HCDR3 and the VL domain comprises LCDR1, LCDR2 and LCDR3, wherein

HCDR1 is of amino acid sequence which has the formula

$$\text{HX}_1 \text{ HX}_2 \text{ G HX}_3 \text{ S}$$

wherein

HX<sub>1</sub> is selected from the group consisting of N, Q, D, L, G and E,

HX<sub>2</sub> is selected from the group consisting of Y and T,

HX<sub>3</sub> is selected from the group consisting of V, I, F and L,

HCDR2 is of amino acid sequence which has the formula

W I HX<sub>4</sub> HX<sub>5</sub> HX<sub>6</sub> HX<sub>7</sub> G HX<sub>8</sub> T HX<sub>9</sub> Y HX<sub>10</sub> HX<sub>11</sub> HX<sub>12</sub> F HX<sub>13</sub> HX<sub>14</sub>  
wherein

HX<sub>4</sub> is selected from the group consisting of S, D, N, A, R, G and E,

HX<sub>5</sub> is selected from the group consisting of A, D, G, T, P, N and Y,

HX<sub>6</sub> is selected from the group consisting of N, D, L, A, P, T, S, I and R,

HX<sub>7</sub> is selected from the group consisting of N, S, T, D, G, K and I,

HX<sub>8</sub> is selected from the group consisting of D, T, E, Q, L, Y, N, V, A, M and G,

HX<sub>9</sub> is selected from the group consisting of N, I, L, Q, S, M, H, D and K,

HX<sub>10</sub> is selected from the group consisting of G and R,

HX<sub>11</sub> is selected from the group consisting of Q and R,

HX<sub>12</sub> is selected from the group consisting of E, K and G,

HX<sub>13</sub> is selected from the group consisting of Q and R,

HX<sub>14</sub> is selected from the group consisting of G and K,

HCDR3 is of amino acid sequence which has the formula

D HX<sub>15</sub> HX<sub>16</sub> HX<sub>17</sub> HX<sub>18</sub> W A R W HX<sub>19</sub> F HX<sub>20</sub> L

wherein

HX<sub>15</sub> is selected from the group consisting of S, R and D,

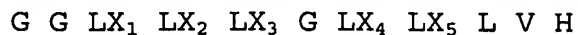
HX<sub>16</sub> is selected from the group consisting of S, N, D, T and P,

HX<sub>17</sub> is selected from the group consisting of S and R,  
HX<sub>18</sub> is selected from the group consisting of S, N, A, I,  
R, P and K,

HX<sub>19</sub> is selected from the group consisting of F and Y,

HX<sub>20</sub> is selected from the group consisting of D and Y,

LCDR1 is of amino acid sequence which has the formula



wherein

LX<sub>1</sub> is selected from the group consisting of N, D and S,

LX<sub>2</sub> is selected from the group consisting of N, I, L, M,  
C, V, K, Y, F, R, T, S, A, H and G,

LX<sub>3</sub> is selected from the group consisting of I and V,

LX<sub>4</sub> is selected from the group consisting of S and G,

LX<sub>5</sub> is selected from the group consisting of K and R,

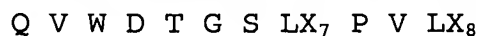
LCDR2 is of amino acid sequence which has the formula



wherein

LX<sub>6</sub> is selected from the group consisting of S and T,

LCDR3 is of amino acid sequence which has the formula



wherein

LX<sub>7</sub> is selected from the group consisting of D and N,

LX<sub>8</sub> is selected from the group consisting of V and I.

63. (original) An isolated specific binding member according to claim 62, wherein

HX<sub>1</sub> is selected from the group consisting of D and N,

HX<sub>2</sub> is Y,

HX<sub>3</sub> is L,

HX<sub>4</sub> is selected from the group consisting of S and G,

HX<sub>5</sub> is selected from the group consisting of T and A,

HX<sub>6</sub> is N,



HX<sub>7</sub> is selected from the group consisting of N and I,  
HX<sub>8</sub> is D,  
HX<sub>9</sub> is selected from the group consisting of N, D and K,  
HX<sub>10</sub> is G,  
HX<sub>12</sub> is selected from the group consisting of E and G,  
HX<sub>13</sub> is Q,  
HX<sub>19</sub> is F,  
LX<sub>1</sub> is selected from the group consisting of N and S,  
LX<sub>2</sub> is selected from the group consisting of N, Y, T, S,  
and I,  
LX<sub>6</sub> is S,  
LX<sub>7</sub> is D.

64. (original) An isolated specific binding member according to claim 62, wherein

HX<sub>1</sub> is selected from the group consisting of N and D,  
HX<sub>2</sub> is Y,  
HX<sub>3</sub> is L,  
HX<sub>4</sub> is selected from the group consisting of S and G,  
HX<sub>5</sub> is selected from the group consisting of A and T,  
HX<sub>6</sub> is N,  
HX<sub>7</sub> is N,  
HX<sub>8</sub> is selected from the group consisting of D and G,  
HX<sub>9</sub> is selected from the group consisting of I, S, N and  
D,  
HX<sub>11</sub> is Q,  
HX<sub>12</sub> is E and K,  
HX<sub>14</sub> is G,  
HX<sub>15</sub> is S,  
HX<sub>16</sub> is selected from the group consisting of S and N,  
HX<sub>17</sub> is S,  
HX<sub>18</sub> is selected from the group consisting of S and N,

HX<sub>19</sub> is F,  
HX<sub>20</sub> is D,  
LX<sub>1</sub> is selected from the group consisting of N and D,  
LX<sub>3</sub> is I,  
LX<sub>8</sub> is V.

65. (original) An isolated specific binding member according to claim 62, wherein

HX<sub>7</sub> is selected from the group consisting of N, S, T, D, G and K,

HX<sub>8</sub> is selected from the group consisting of D, T, E, Q, L, Y, N, V, A, M,

HX<sub>9</sub> is selected from the group consisting of N, I, L, Q, S, M and H,

HX<sub>10</sub> is G,

HX<sub>11</sub> is Q,

HX<sub>12</sub> is F,

HX<sub>13</sub> is Q,

HX<sub>14</sub> is G,

HX<sub>15</sub> is S,

HX<sub>16</sub> is selected from the group consisting of N and S,

HX<sub>17</sub> is S,

HX<sub>18</sub> is selected from the group consisting of N and S,

HX<sub>19</sub> is F,

HX<sub>20</sub> is D,

LX<sub>1</sub> is N,

LX<sub>2</sub> is selected from the group consisting of N and I,

LX<sub>3</sub> is I,

LX<sub>4</sub> is S,

LX<sub>5</sub> is K,

LX<sub>6</sub> is S,

LX<sub>7</sub> is D,

LX<sub>8</sub> is V.

66. (original) An isolated specific binding member according to claim 65, wherein

HX<sub>1</sub> is selected from the group consisting of N, Q and D,

HX<sub>3</sub> is selected from the group consisting of L, V and I,

HX<sub>4</sub> is selected from the group consisting of S, N, A and R,

HX<sub>5</sub> is selected from the group consisting of A, D, T, G, N and Y,

HX<sub>6</sub> is selected from the group consisting of N, A, P, S, D and I,

HX<sub>7</sub> is selected from the group consisting of N, T, D and G,

HX<sub>8</sub> is selected from the group consisting of D, Q, Y and N,

HX<sub>9</sub> is selected from the group consisting of N, Q, S and I.

67. (currently amended) A specific binding member according to claim 62~~any one of claims 62 to 66~~ that neutralizes human IL-13.

68. (original) A specific binding member according to claim 67 that neutralizes human IL-13, with a potency equal to or better than the potency of a IL-13 antigen-binding site formed by the BAK502G9 VH domain (SEQ ID NO: 15) and the BAK502G9 VL domain (SEQ ID NO: 16), the potency of the specific binding member and the potency of the antigen-binding site being as determined under the same conditions.

69. (currently amended) A specific binding member according to claim 62~~any one of claims 62 to 68~~ that comprises an scFv antibody molecule.

70. (currently amended) A specific binding member according

to claim 62~~any one of claims 62 to 68~~ that comprises an antibody constant region.

71. (original) A specific binding member according to claim 70 that comprises a whole antibody.

72. (original) A specific binding member according to claim 71 wherein the whole antibody is IgG4.

73. (currently amended) An isolated specific binding member according to ~~any one of claims 62 to 72~~claim 62 which binds a human IL-13 variant in which arginine at position 130 is replaced by glutamine.

74. (currently amended) An isolated specific binding member according to claim 62~~any one of claims 62 to 72~~ which binds non-human primate IL-13.

75. (original) An isolated specific binding member according to claim 74 wherein the non-human primate IL-13 is rhesus or cynomolgus.

76. (currently amended) An isolated antibody VH domain of a specific binding member according to claim 62~~any one of claims 62 to 75~~.

77. (currently amended) An isolated antibody VL domain of a specific binding member according to claim 62~~any one of claims 62 to 75~~.

78. (currently amended) A composition comprising the specific binding, antibody VH domain or antibody VL domain of claim 62~~any one of claims 62 to 77~~, and at least one

additional component.

79. (original) A composition according to claim 78 comprising a pharmaceutically acceptable excipient, vehicle or carrier.

80. (currently amended) An isolated nucleic acid which comprises a nucleotide sequence encoding a specific binding member or antibody VH or VL domain of a specific binding member according to claim 62~~any one of claims 62 to 77~~.

81. (original) A host cell *in vitro* transformed with nucleic acid according to claim 80.

82. (original) A method of producing a specific binding member or antibody VH or VL domain, the method comprising culturing host cells according to claim 81 under conditions for production of said specific binding member or antibody VH or VL domain.

83. (original) A method according to claim 82 further comprising isolating and/or purifying said specific binding member or antibody VH or VL variable domain.

84. (currently amended) A method according to claim 82 ~~or claim 83~~ further comprising formulating the specific binding member or antibody VH or VL variable domain into a composition including at least one additional component.

85. (currently amended) A method according to claim 82~~any one of claims 82 to 84~~ further comprising binding a specific binding member that binds human IL-13 to IL-13 or a fragment

of IL-13.

86. (currently amended) A method comprising binding a specific binding member that binds IL-13 according to claim 62~~any one of claims 62 to 75~~ to human IL-13 or a fragment of human IL-13.

87. (currently amended) A method according to claim 85 ~~or claim 86~~ wherein said binding takes place *in vitro*.

88. (currently amended) A method according to claim 85~~any one of claims 85 to 87~~ comprising determining the amount of binding of specific binding member to IL-13 or a fragment of IL-13.

89. (currently amended) A method according to claim 82~~any one of claims 82 to 84~~ further comprising use of the specific binding member in the manufacture of a medicament for treatment of a disease or disorder selected from the group consisting of asthma, atopic dermatitis, allergic rhinitis, fibrosis, inflammatory bowel disease and Hodgkin's lymphoma.

90. (currently amended) Use of a specific binding member according to claim 62~~any one of claims 62 to 75~~ in the manufacture of a medicament for treatment of a disease or disorder selected from the group consisting of asthma, atopic dermatitis, allergic rhinitis, fibrosis, inflammatory bowel disease and Hodgkin's lymphoma.

91. (currently amended) A method of treatment of a disease or disorder selected from the group consisting of asthma, atopic dermatitis, allergic rhinitis, fibrosis and Hodgkin's

lymphoma, the method comprising administering a specific binding member according to claim 62~~any one of claims 62 to 75~~ to a patient with the disease or disorder or at risk of developing the disease or disorder.